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Management of Adenocarcinoma of the Body and Tail of the Pancreas

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Objective
The authors examined the resectability, operative morbidity, mortality, and survival of patients with pancreatic adenocarcinoma of the body and tail compared with lesions in the head.

Summary Background Data
Adenocarcinoma of the body and tail of the pancreas is characteristically thought of as a disease that presents late and rarely is operable or resectable.

Methods
In an 11-year period, 1981 patients were admitted and entered into a prospective database at Memorial Sloan-Kettering Cancer Center with a diagnosis of peripancreatic cancer, 1363 of whom had adenocarcinoma of the pancreas, 75% with lesions in the head and 25% with lesions in the body and tail.

Results
Of 271 patients resected, 237 (23%) had lesions in the head and 34 (10%) had body and tail lesions. Perioperative mortality was 4% for patients with pancreatic lesions in the head and 0% for patients with pancreatic lesions in the body and tail. Five-year actuarial survival for body and tail lesions was projected at 14% for 5 years. Actual survival was 19%, with three patients alive for more than 5 years.

Conclusions
Adenocarcinoma of the body and tail of the pancreas, although less likely to be resectable at presentation than lesions in the pancreatic head, have similar postresection survival.

Historically, adenocarcinoma of the body and tail of the pancreas has been considered a disease with poor prognosis, with very few, if any, long-term survivors.[1] The tumor is thought to occur less frequently in the body and tail than the head of the gland, and to present later, with more advanced disease. It was concluded in 1989 that fewer than five patients had been reported to have lived 5 years after diagnosis.[2,3] However, three recent papers from major institutions have documented isolated patients who are long-term survivors.[4–6]

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MATERIALS AND METHODS

In October 1983, we began a prospective database of all patients admitted with suspected or confirmed peri-

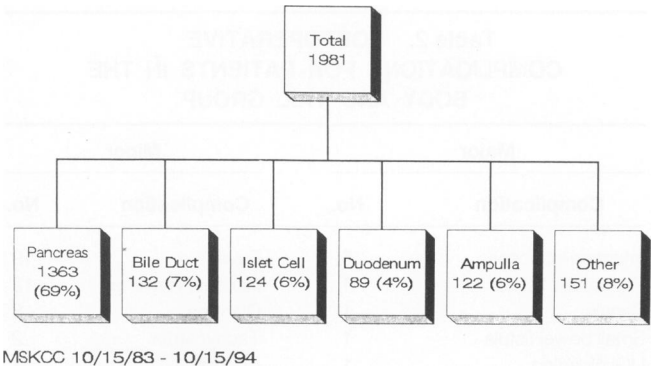

Figure 1. Sites for 1981 patients admitted to Memorial Sloan-Kettering Cancer Center from October 15, 1983, to October 15, 1994, with diagnoses of peripancreatic cancer.

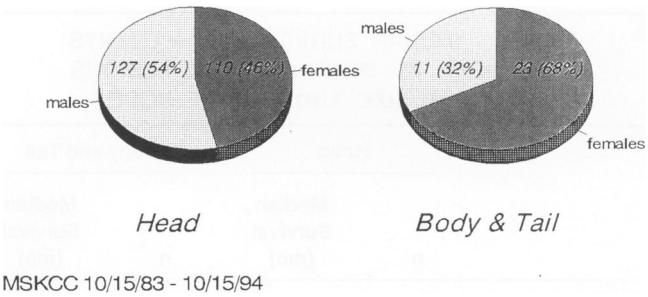

Figure 2. Gender of patients who were resected: head *vs.* body and tail lesions.

pancreatic malignancy (adenocarcinoma of distal bile duct, pancreas, ampulla, duodenum, islet cell tumors and other rare malignancies; Fig. 1). Between October 1983 and October 1994, 1981 patients were admitted; of these, 1363 were diagnosed with classical adenocarcinoma of the pancreas. The dominant site of origin for the tumor was not determined in five patients who did not undergo resection. Patients with squamous carcinoma, cystadenocarcinoma, metastatic disease to the pancreas, papillary carcinoma, and other rare malignancies of the pancreas were excluded from the analysis and are included with "other" in Figure 1. Two hundred seventy one patients with classical adenocarcinoma of the pancreas were resected and analyzed for resectability, operative mortality, and long-term outcome. Of these, 237 had lesions in the head of the pancreas, and 34 had lesions in the body and tail. Median follow-up for surviving patients who underwent resection of the pancreatic head was 14.6 months; for resection of the body and tail, median follow-up was 22 months. Survival was calculated using the Kaplan-Meier method, using the log-rank test for comparison of differences in survival. Cox proportional hazards regression analysis was used to determine independent prognostic indicators. The Wilcoxon rank sum test was used to compare differences between the median length of stay and the number of lymph nodes examined. A two-tailed Student's t test for equality of means was used for size comparison.

RESULTS—RESECTIONS

Demographics

Of all patients admitted, lesions arising in the head of the pancreas were three times as common as lesions of the body and tail. There were twice as many women as men in the body and tail group, whereas the male:female ratio for lesions of the head was 1.2:1 (Fig. 2). The distribution by age is shown in Figure 3. Seventy-nine percent of the patients in both groups were 55 years of age or older, and the mean age was 63 years.

Size

Lesions in the body and tail of the pancreas were more often large (> 2 cm) than lesions in the head (85% *vs.* 78%; Table 1). The means were 4.9 ± 2.4 cm in greatest diameter for lesions in the body and tail group and 3.4 ± 1.6 cm for lesions in the head. Using a two-tailed Student's t test for equality of means, a significant difference between the two groups was demonstrated ($p = 0.001$).

Resectability

Of 331 patients with adenocarcinoma of the body and tail of the pancreas, 10% (34) underwent resection; 237 of the 1027 patients with carcinoma of the head of the pancreas (23%) underwent resection (Fig. 4). Within the body and tail group, 3 of 34 (9%) underwent total pancreatectomies.

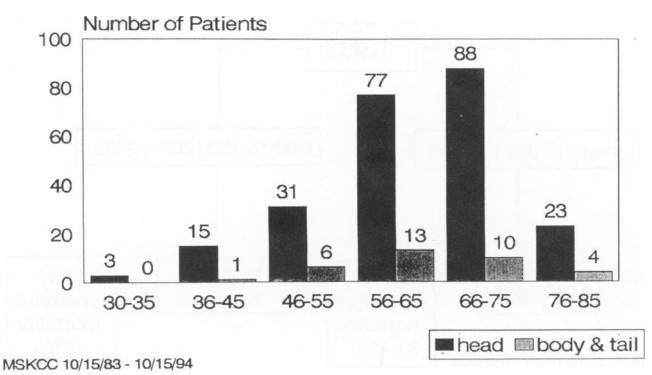

Figure 3. Resected patients—distribution of patients by age for head and body and tail lesions.

Table 1. MEDIAN SURVIVAL OF PATIENTS WITH HEAD *VS.* BODY AND TAIL LESIONS BY TUMOR SIZE AND SIZE OF NODES

	Head		Body and Tail	
	n	Median Survival (mo)	n	Median Survival (mo)
Overall				
≤2 cm	51	24.2	5	59.8
>2 cm	186	14.9	29	10.4
Negative nodes				
≤2 cm	18	37.1	2	59.8
>2 cm	92	15.7	16	10.4
Positive nodes				
≤2 cm	33	22.2	3	20
>2 cm	94	12.5	13	8

Operative Mortality and Morbidity

There was no perioperative death in the body and tail group, and nine of those with lesions in the head of the pancreas (3.8%) died within 30 days of operation (Fig. 4). Postoperative complications for the patients in the body and tail group are listed in Table 2. Major perioperative morbidity, *i.e.*, patients experiencing one or more major complications, was 23% (8/34). Three patients (8.6%) required re-exploration for drainage of abscesses; one of these patients required a second re-exploration.

Length of Stay

Table 3 shows the overall and postoperative mean, median, and range for length of stay. Patients with body and tail lesions had a statistically significant decrease in postoperative length of stay compared with patients with pancreatic head lesions (p = 0.02).

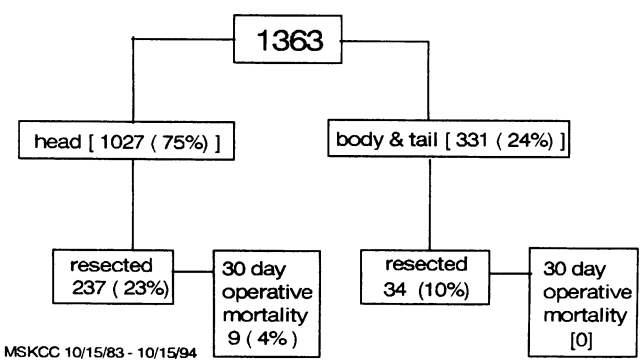

Figure 4. Resections and 30-day operative mortality in head and body and tail lesions (five were unknown sites).

Table 2. POSTOPERATIVE COMPLICATIONS FOR PATIENTS IN THE BODY AND TAIL GROUP

Major		Minor	
Complication	No.	Complication	No.
Infection/abscess	6	Fever	19
Pancreatic fistula	1	Nausea/vomiting	12
Sepsis	1	Diarrhea	8
Small bowel fistula	1	Tachycardia	2
UGI bleeding	1	Edema	1
Small bowel obstruction	1	Ileus	1
		Respiratory	1

UGI = upper gastrointestinal.

Survival

Overall survival is illustrated in Figure 5. Median survival was 16.3 months for patients with head lesions, 12 months for patients with body and tail lesions. There was no difference in long- term survival between the resected groups. For patients who did not undergo resection, median survival was 5.2 months. Although long-term survival is rare, three patients in the body and tail group are alive longer than 5 years.

Survival by size is shown in Figure 6. Patients with smaller lesions in both groups (≤ 2 cm) did much better than patients with larger tumors, and a significant difference as shown between the two groups (p = 0.0005).

Lymph Node Involvement

The mean, median, and range of the number of lymph nodes is shown in Table 4 and is similar for both groups. There was no statistically significant difference in median nodes examined between the two groups. The prevalence of node positivity was highly dependent on the vigor with which nodes were examined. However, the

Table 3. PANCREATIC ADENOCARCINOMA: RESECTIONS ([LENGTH OF STAY [DAYS]])

	n	Mean	Median	Range
Overall				
Head	237	25.5	22	3–131
Body and tail	34	20.8	15.5	8–89
Postoperative				
Head	237	21.2	17	0–125
Body and tail	34	17.9	13.5	7–88

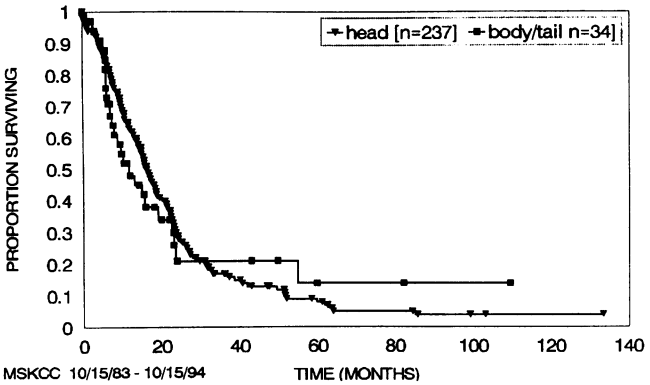

Figure 5. Overall survival for patients having resections. There was no difference in long-term survival between the sites.

relative prevalence of negative nodes was remarkably similar, *i.e.*, approximately 50% of resected patients—whether the lesion arose in the head, body, or tail of the pancreas—were found to have positive nodes, suggesting relatively uniform pathologic examination of the specimens.

Table 5 shows the distribution and median survival by relative number of lymph node metastases by site. The presence of positive or negative nodes did influence overall survival (p = 0.04), but there was no difference between the two sites (Fig. 7). Size was not a factor in the likelihood of a positive node (Table 1). Overall, 64% of patients with lesions ≤ 2 cm (36/56) and 50% with lesions > 2 cm (107/215) had positive nodes. The combination of small size and negative nodes translated into a very significant survival advantage (p = 0.0001). Median survival for patients with smaller tumors and negative nodes was 40.5 months compared with 12.5 months for patients with larger tumors and nodal metastases.

Margins

Surgical margins were a significant factor in overall survival. Median survival for patients with positive microscopic margins was 10.4 months; for patients with negative margins, median survival was 17.1 months (p = 0.02, Fig. 8). However, no significant difference in outcome was found when body and tail lesions were compared with head lesions (Fig. 9). The frequency of positive margins was higher in body and tail lesions than in head lesions (32% *vs.* 21%).

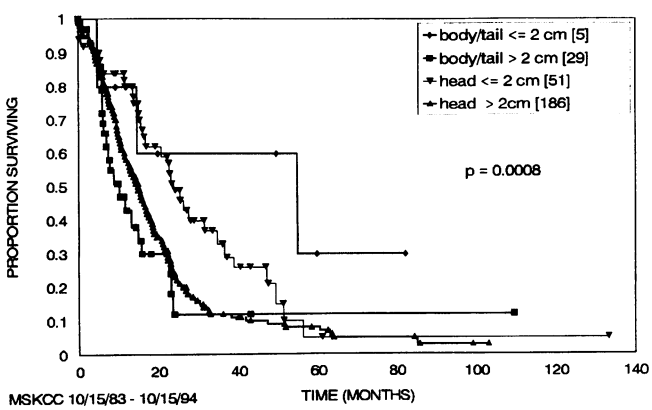

Figure 6. Size was a significant factor in survival in both sites (p = 0.0008).

Table 4. DISTRIBUTION OF NODAL METASTASES: NUMBER OF NODES EXAMINED*

Site	Mean	Median	Range
Head	19.5	16	0–83
Body and tail	17.5	13	1–72

* p = 0.1 (Wilcoxon rank sum W test).

Histologic Differentiation

Histologic differentiation was analyzed for patients in the body and tail group (Fig. 10). A significant difference in survival was found when poorly differentiated tumors were compared with well-differentiated tumors (p = 0.05). Median survival was 6.5 months for patients with poorly differentiated tumors and 23.1 months for those with well-differentiated tumors.

Eight of the 34 patients (23.5%) with body and tail lesions were histologically poorly differentiated adenosquamous carcinomas, and survival for these patients was significantly worse (p = 0.02). The median survival was 7 months compared with 15.9 months for the other 26 patients.

Table 5. ADENOCARCINOMA OF THE PANCREAS—MEDIAN SURVIVAL (MONTHS) BY RELATIVE NUMBER OF NODES

	No. of Positive Nodes			
	0	1	2–5	>5
Overall (n = 271)				
n	128	50	77	16
Median survival (mo)	17.1	16.1	16.5	9.8
Body and tail (n = 34)				
n	18	5	10	1
Median survival (mo)	12	8	14.3	49.7 (not median)
Head (n = 237)				
n	110	45	67	15
Median survival (mo)	17.5	16.8	16.7	9.8

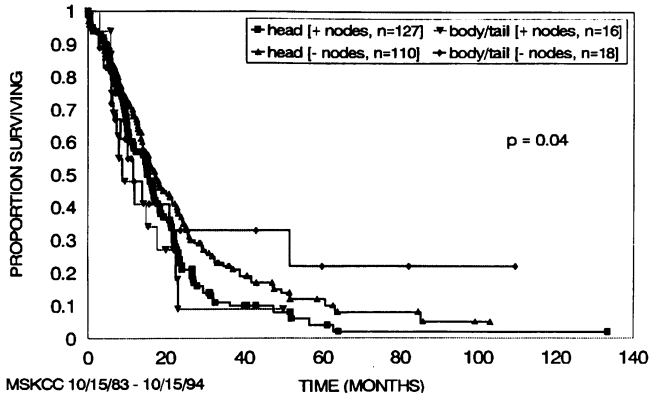

Figure 7. Although the presence of positive or negative nodes influenced survival (p = 0.04); there was no difference between the sites.

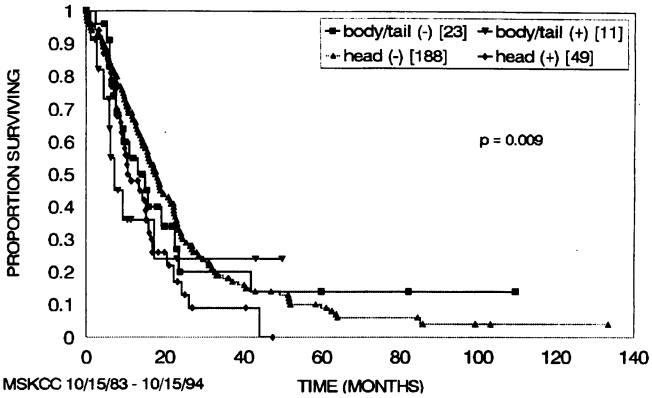

Figure 9. Survival by microscopic margins according to site. No significant difference in outcome was found when body and tail lesions were compared with head lesions.

DISCUSSION

Most series suggest that adenocarcinoma of the pancreas is less common in the body and tail than in the head of the pancreas. However, given the relative volume of each part of the pancreas,[7] the distribution probably is proportionate. In those series that have been reported, operative mortality has been low (Table 6), consistent with improved overall mortality after resection for all adenocarcinomas of the pancreas in recent years.[8] In the current reported series of 34 patients resected during the last 11 years, the resectability rate of 10% is similar to that reported by other authors.

The resectability rate for body and tail lesions is less than one half of the resectability rate for lesions of the head, which are presumed to present earlier. Nevertheless, as the worldwide resectability rates increase, with better preoperative selection including helical computed tomography and laparoscopy, the resectability rate will continue to be less for body and tail lesions than for head lesions.

In the recent analysis of patients from three major institutions, only three 5-year survivors have been reported from a cohort of 48 patients (Table 6). Three of the present 34 have lived or are alive beyond 5 years, and another is alive with no evidence of disease at 50 months.

Node positivity usually is considered a powerful factor in predicting outcome for resections of adenocarcinoma of the pancreas, regardless of site, with very rare, isolated patients living with positive nodes. In the current series, we have not yet had a 5-year survivor with a discontiguous positive node associated with a body or tail lesion. However, overall the number of nodes involved did not appear to have a major impact on survival (Table 5), perhaps emphasizing the overall palliative aspect of resection for this disease, for which so few long-term survivors exist that the negative impact of prognostic factors such as the nodes found and proven to be positive are minimal.

Size, surgical margins of resection, and nodal metastases all are independent significant factors for predicting outcome with regard to overall survival. Significance

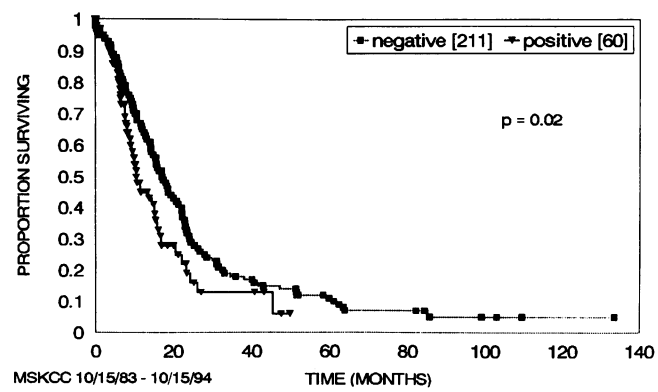

Figure 8. Overall survival by microscopic margins for resections in adenocarcinoma of the pancreas. Median survival for patients with positive microscopic margins was 10.4 months, compared with 17.1 months for negative margins.

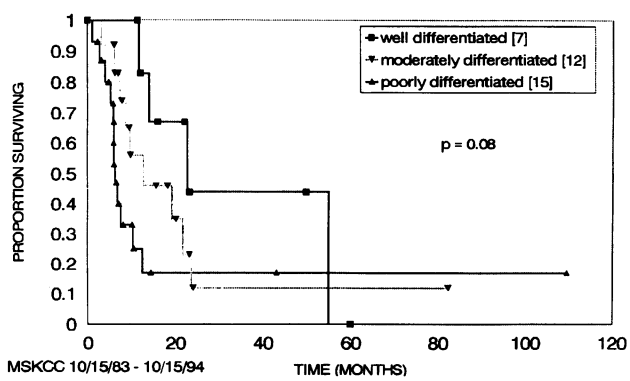

Figure 10. Survival by histologic differentiation for patients with body and tail lesions.

Table 6. ADENOCARCINOMA OF THE BODY AND TAIL OF THE PANCREAS IN SEVERAL SERIES

Location	Reference (year)	No. of Years	Total No.	No. Resected (%)	Operative Mortality	Median Survival (%)	Projected 5-yr Survival (%)	Projected 2-yr Survival (%)
Johns Hopkins	Nordback[6] (1992)	17	113	9 (8)	0	7	11	22
Mannheim	Johnson[5] (1993)	17	105	13 (12)	0	13	0	38
Mayo Clinic	Dalton[4] (1992)	25		26	0	10	8	15
MSKCC	Present series	11	331	34 (10)	0	12	14 (19)*	15 (23)*

* Actual survival.

among these factors could not be shown within the body and tail group because of the small number of patients in this series. The only significant factor with regard to survival within the body and tail group was histologic differentiation, when comparing well and poorly differentiated tumors ($p = 0.05$).

The current analysis suggests that in patients with body and tail pancreatic lesions, the same approach to resection should be applied as is done for lesions of the head, *i.e.*, for patients without known metastatic disease or major vascular invasion, surgery should be contemplated seriously as the best currently available therapeutic approach; however, as with the majority of patients with adenocarcinoma of the pancreas in any site, it should be a palliative procedure.

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Discussion

DR. ANDREW L. WARSHAW (Boston, Massachusetts): Thank you again, Mr. President. I apologize for the accident of being up here twice in a row, which is a function of a change in the program.

Dr. Brennan has pointed out that, as a number of series have called to our attention, and none better than this, that adenocarcinoma of the tail of the pancreas is a potentially resectable lesion. I spent many years thinking that this was not true and had also challenged for many years someone to come up with a long-term survivor. And, clearly, both of these challenges have been met.

The issue, though, is are we painting it a little too pink when we say it is 10% resectability. This is a preselected group of patients who have already been screened by computed tomography (CT) scan or ultrasound or a variety of other possible measures. And the good ones are selected out for potential exploration.

So the first question for Dr. Brennan is, going forward from here, knowing that you can do it, what will you do to enhance your selection process, perhaps to operate on fewer patients who will not benefit from the operation?

You mentioned laparoscopy in passing. Sixty percent of our patients with body and tail lesions who undergo laparoscopy after negative CT scans have positive demonstration of metastatic disease, which, therefore, eliminates, in our hands at least, the need for or the benefit of laparotomy. Is helical CT scan, spiral CT scan, which may be the best staging tool we have today, useful in picking out these tumors, especially in terms of the retroperitoneal extension that concerns Dr. Brennan?

A big question about this experience, as with the Hopkins experience previously presented to us, is just how much disease is acceptable. In going in there if you found the tumor small and a chip shot, that is easy. If you found it kind of stuck posteriorly, how are you willing to cut across tumor to get an effective debulking procedure? Does that do harm by spreading tumor, or does it do potential good by reducing the target for chemoradiation adjunctively postoperatively and, therefore, provide benefit?

Do you assume, Dr. Brennan, that most of these patients are in fact being palliated, that they will have local recurrence and perhaps, therefore, the problem of duodenal obstruction, which is one of the major morbidities of advanced pancreatic carcinoma in the body and tail. Should you, therefore, relatively routinely or based on some specific criteria, do a gastrojejunostomy even if you are doing the distal pancreatectomy?

I really enjoyed this paper. It tells us again where we can do